09/941,882

[redacted]

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FILE 'HOME' ENTERED AT 15:52:35 ON 15 JUL 2003

=> file biosis medline caplus wpids uspatfull

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'BIOSIS' ENTERED AT 15:52:59 ON 15 JUL 2003

FILE 'MEDLINE' ENTERED AT 15:52:59 ON 15 JUL 2003

FILE 'CAPLUS' ENTERED AT 15:52:59 ON 15 JUL 2003

FILE 'WPIDS' ENTERED AT 15:52:59 ON 15 JUL 2003

FILE 'USPATFULL' ENTERED AT 15:52:59 ON 15 JUL 2003

*** YOU HAVE NEW MAIL ***

=> s nucleic acid? sequencing
L1 2960 NUCLEIC ACID? SEQUENCING

=> s l1 and heat
L2 1048 L1 AND HEAT

=> s l2 and diphenyliodonium
L3 1 L2 AND DIPHENYLIODONIUM

=> d l3 bib abs

L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN 2002:736776 CAPLUS
DN 137:258477
TI Real-time **nucleic acid sequencing** by monitoring of labeled base incorporation followed by removal and substitution of the labeled nucleotide
IN Williams, Peter; Taylor, Thomas J.; Williams, Daniel J. B.; Gould, Ian; Hayes, Mark A.
PA USA
SO U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U.S. Ser. No. 673,544. CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002137062	A1	20020926	US 2001-941882	20010828
	WO 9957321	A1	19991111	WO 1999-US9616	19990430

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

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     WO 2003020895     A2   20030313      WO 2002-US27605  20020828
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
PRAI US 1998-83840P     P    19980501
     WO 1999-US9616     A2   19990430
     US 2001-673544     A2   20010226
     US 2001-941882     A    20010828
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AB The present invention relates to a novel method for analyzing nucleic acid sequences based on real-time detection of DNA polymerase-catalyzed incorporation of each of the four nucleotide bases, supplied individually and serially in a microfluidic system, to a reaction cell contg. a template system comprising a DNA fragment of unknown sequence and an oligonucleotide primer. Incorporation of a nucleotide base into the template system can be detected by any of a variety of methods including but not limited to fluorescence and chemiluminescence detection. Alternatively, microcalorimetric detection of the **heat** generated by the incorporation of a nucleotide into the extending template system using thermopile, thermistor and refractive index measurements can be used to detect extension reactions. The preferred method uses a two-stage primer extension procedure. In the first stage the primer is extended by exposing it to labeled derivs. of nucleotide triphosphates in the presence of an exonuclease free DNA polymerase until a signal indicating incorporation is seen. THe labeled nucleotide is removed and replaced using the correctly identified nucleotide and a mixt. of DNA polymerases with and without exonuclease activity. The use of microcalorimetry to detect base incorporation is demonstrated. The use of **diphenyliodonium** to bleach fluorescent labels is demonstrated.

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     (FILE 'HOME' ENTERED AT 15:52:35 ON 15 JUL 2003)

     FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 15:52:59 ON
     15 JUL 2003
L1          2960 S NUCLEIC ACID? SEQUENCING
L2          1048 S L1 AND HEAT
L3             1 S L2 AND DIPHENYLIODONIUM

=> s l2 and pyrophosphate
L4           228 L2 AND PYROPHOSPHATE

=> s l4 and hydrolosis (4a) pyrophosphate
L5             0 L4 AND HYDROLOSIS (4A) PYROPHOSPHATE

=> s l4 and hydroly? (4a) pyrophosphate
L6             3 L4 AND HYDROLY? (4A) PYROPHOSPHATE

=> d l6 bib abs 1-3

L6   ANSWER 1 OF 3  USPATFULL
AN     2003:86313  USPATFULL
TI     Novel human 39228, 21956, 25856, 22244, 8701, 32263, 50250, 55158,
       47765, 62088, 50566, and 48118 molecules and uses therefor
```

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IN Meyers, Rachel E., Newton, MA, UNITED STATES
Rudolph-Owen, Laura A., Jamaica Plain, MA, UNITED STATES
Kapeller-Libermann, Rosana, Chestnut Hill, MA, UNITED STATES
PA Millennium Pharmaceuticals, Inc., Cambridge, MA, UNITED STATES, 02139 (U.S. corporation)
PI US 2003059919 A1 20030327
AI US 2002-160501 A1 20020530 (10)
RLI Continuation-in-part of Ser. No. US 2001-838573, filed on 18 Apr 2001, PENDING Continuation-in-part of Ser. No. US 2001-870133, filed on 29 May 2001, PENDING Continuation-in-part of Ser. No. US 2001-870130, filed on 29 May 2001, PENDING Continuation-in-part of Ser. No. US 2001-862535, filed on 21 May 2001, PENDING Continuation-in-part of Ser. No. US 2001-870383, filed on 29 May 2001, PENDING Continuation-in-part of Ser. No. US 2001-860821, filed on 18 May 2001, PENDING Continuation-in-part of Ser. No. US 2001-870110, filed on 29 May 2001, PENDING Continuation-in-part of Ser. No. US 2001-907509, filed on 16 Jul 2001, PENDING Continuation-in-part of Ser. No. US 2001-945327, filed on 31 Aug 2001, PENDING
PRAI US 2000-197747P 20000418 (60)
US 2000-207649P 20000526 (60)
US 2000-207640P 20000526 (60)
US 2000-205961P 20000519 (60)
US 2000-207506P 20000526 (60)
US 2000-205449P 20000519 (60)
US 2000-207650P 20000526 (60)
US 2000-218385P 20000714 (60)
US 2000-229425P 20000831 (60)
US 2001-318581P 20010910 (60)
DT Utility
FS APPLICATION
LREP LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 100 Drawing Page(s)
LN.CNT 44311
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides isolated nucleic acids molecules, designated 39228, 21956, 25856, 22244, 8701, 32263, 50250, 55158, 47765, 62088, 50566, and 48118 nucleic acid molecules, which encode novel GTPase activating molecules, cadherin molecules, and ankyrin containing family members. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing 39228, 21956, 25856, 22244, 8701, 32263, 50250, 55158, 47765, 62088, 50566, and 48118 nucleic acid molecules, host cells into which the expression vectors have been introduced, and non-human transgenic animals in which a 39228, 21956, 25856, 22244, 8701, 32263, 50250, 55158, 47765, 62088, 50566, or 48118 gene has been introduced or disrupted. The invention still further provides isolated 39228, 21956, 25856, 22244, 8701, 32263, 50250, 55158, 47765, 62088, 50566, and 48118 polypeptides, fusion polypeptides, antigenic peptides and anti-39228, 21956, 25856, 22244, 8701, 32263, 50250, 55158, 47765, 62088, 50566, and 48118 antibodies. Diagnostic and therapeutic methods utilizing compositions of the invention are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 2 OF 3 USPATFULL
AN 2001:67439 USPATFULL
TI Mutant chimeric DNA polymerase
IN Gelfand, David Harrow, Oakland, CA, United States
Reichert, Fred Lawrence, Oakland, CA, United States
PA Roche Molecular Systems, Pleasanton, CA, United States (U.S.

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       corporation)
PI     US 6228628        B1   20010508
AI     US 1998-105697         19980626 (9)
PRAI   US 1997-52065P       19970709 (60)
DT     Utility
FS     Granted
EXNAM  Primary Examiner: Achutamurthy, Ponnathapu; Assistant Examiner: Hutson,
       Richard
LREP   Petry, Douglas A.
CLMN   Number of Claims: 63
ECL    Exemplary Claim: 1
DRWN   3 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 2195
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     Mutant, chimeric thermostable DNA polymerases are provided, along with
       purified DNA sequences that encode the enzymes. Also provided are
       methods for producing and using the enzymes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 3 OF 3  USPATFULL
AN     97:81103  USPATFULL
TI     Purified nucleic acid encoding a thermostable pyrophosphatase
IN     Gelfand, David Harrow, Oakland, CA, United States
       Wang, Alice Ming, Lafayette, CA, United States
PA     Roche Molecular Systems, Inc., Branchburg, NJ, United States (U.S.
       corporation)
PI     US 5665551             19970909
AI     US 1995-528384         19950913 (8)
DT     Utility
FS     Granted
EXNAM  Primary Examiner: Hendricks, Keith D.
LREP   Johnston, George W., Sias, Stacey R., Petry, Douglas A.
CLMN   Number of Claims: 7
ECL    Exemplary Claim: 7
DRWN   No Drawings
LN.CNT 921
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     Purified DNA sequences that encode a thermostable pyrophosphatase are
       provided. The purified DNA is obtained using a DNA probe consisting of
       SEQ ID NO: 1. Also provided are methods for producing thermostable
       pyrophosphatase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.


=> d l6 2-3 kwic

L6    ANSWER 2 OF 3  USPATFULL
SUMM   . . . polymerase, methods for its synthesis, and methods for its use.
       The enzyme is useful in many recombinant DNA techniques, especially
       nucleic acid sequencing and nucleic acid
       amplification by the polymerase chain reaction (PCR).
SUMM   Typically, sequencing by the chain termination method is carried out
       using repeated steps of primer extension followed by heat
       denaturation of the primer extension product-template duplex. This
       embodiment, referred to as cycle sequencing, is carried out in a
       thermal. . .
DETD   The term "thermostable enzyme", as used herein, refers to an enzyme
       which is stable to heat and has an elevated temperature
       reaction optimum. The thermostable enzyme of the present invention
       catalyzes primer extension optimally at a. . .
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DETD . . . catalyze the template-dependent incorporation of a deoxynucleotide onto the 3'-hydroxyl terminus of a primer, with the concomitant release of inorganic **pyrophosphate** (PPi). This polymerization reaction is reversible. DNA polymerases also catalyze the reverse reaction, pyrophosphorolysis, which is the degradation of DNA. . .

DETD Inorganic pyrophosphatase (PPase), also known as **pyrophosphate** phosphohydrolase, catalyzes **hydrolysis** of inorganic **pyrophosphate** (PPi) to two molecules of orthophosphate. PPase plays an vital role in RNA and DNA synthesis in vivo. By cleaving. . .

DETD . . . such as those derived from polyoma, adenovirus 2, bovine papilloma virus (BPV), or avian sarcoma viruses, or immunoglobulin promoters and **heat** shock promoters. A system for expressing DNA in mammalian systems using a BPV vector system is disclosed in U.S. Pat.. . .

DETD . . . polymerase is carried out in E. coli, which is a mesophilic bacterial host cell. Because E. coli host proteins are **heat** -sensitive, the recombinant thermostable DNA polymerase can be substantially enriched by **heat** inactivating the crude lysate. This step is done in the presence of a sufficient amount of salt (typically 0.2-0.4 M. . .

DETD C. The amplified products from steps A and B are combined, **heat** denatured at 95.degree. C., annealed, and extended with DNA polymerase using standard techniques.

DETD C. The amplified products from steps A and B were combined, **heat** denatured at 95.degree. C., annealed, and extended with DNA polymerase using standard techniques.

DETD Ammonium sulfate was added to the Fraction II supernatant to a concentration of 0.4 M. Fraction II then was **heat**-treated as follows.

DETD The **heat** treatment was carried out in a 3 liter Braun fermentor. The agitation rate was 250 rpm. The temperature was increased. . . over 6 minutes, held for 15 minutes, then cooled in the fermentor to 30.degree. C. as rapidly as possible. The **heat** -treated Fraction II supernatant from the PEI precipitation was removed from the fermentor and held on ice for at least 30. . .

DETD . . . as a carrier. The DNA was precipitated by the addition of 1 ml 20% trichloroacetic acid (w/v) and 2% sodium **pyrophosphate**, and incubated at 0.degree. C. for 15 minutes. Precipitated DNA was collected on GF/C filter discs (Whatman International Ltd., Maidstone, England) and washed extensively with 5% trichloroacetic acid and 2% sodium **pyrophosphate**, then with 5% trichloroacetic acid, then with 5 ml of 95% ethanol, dried, and counted.

L6 ANSWER 3 OF 3 USPATFULL

SUMM . . . relates to the in vitro synthesis of a thermostable pyrophosphatase. Thermostable pyrophosphatases are useful in many recombinant DNA techniques, especially **nucleic acid sequencing** and nucleic acid amplification by the polymerase chain reaction (PCR).

SUMM **Pyrophosphate** is a common product of biosynthetic reactions. Inorganic pyrophosphatase (PPase), also known as **pyrophosphate** phosphohydrolase, catalyzes **hydrolysis** of inorganic **pyrophosphate** (PPi) to two molecules of orthophosphate. PPase plays an vital role in RNA and DNA synthesis in vivo. By cleaving. . .

SUMM . . . between 25 and 40 times. Initial amplification conditions are chosen which favor the forward (polymerization) reaction (high dNTP concentrations, low **pyrophosphate** concentration). However, the amplification reaction results in an accumulation of **pyrophosphate** which increases the rate of the reverse reaction (pyrophosphorolysis), thereby decreasing the overall efficiency of the amplification reaction.

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SUMM The term "thermostable enzyme", as used herein, refers to an enzyme which is stable to **heat** and has an elevated temperature reaction optimum. The thermostable pyrophosphatase encoded by the nucleic acid sequence of the present invention. . .

SUMM . . . such as those derived from polyoma, adenovirus 2, bovine papilloma virus (BPV), or avian sarcoma viruses, or immunoglobulin promoters and **heat** shock promoters. A system for expressing DNA in mammalian systems using a BPV vector system is disclosed in U.S. Pat.. . .

SUMM . . . PPase is carried out in E. coli, which is a mesophilic bacterial host cell. Because E. coli host proteins are **heat** -sensitive, the recombinant thermostable PPase can be substantially enriched by **heat** inactivating the crude lysate. This step is done in the presence of a sufficient amount of salt (typically 0.3M ammonium. . .

SUMM Activity of the purified PPase is assayed as follows. The purified enzyme is used in the **hydrolysis** of inorganic **pyrophosphate** (PPi) with subsequent release of two orthophosphates, and resulting amount of orthophosphate is measured. The hydrolysis reaction is carried out. . .

DETD . . . duty cycle for 3 minutes to reduce the viscosity. The sonicate was heated at 85.degree. C. for 15 minutes. The **heat**-treated supernatant was chilled rapidly to 0.degree. C., and the E. coli cell membranes and denatured proteins were removed following centrifugation. . .

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     (FILE 'HOME' ENTERED AT 15:52:35 ON 15 JUL 2003)

     FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 15:52:59 ON
     15 JUL 2003
L1          2960 S NUCLEIC ACID? SEQUENCING
L2          1048 S L1 AND HEAT
L3             1 S L2 AND DIPHENYLIODONIUM
L4           228 S L2 AND PYROPHOSPHATE
L5             0 S L4 AND HYDROLOSIS (4A) PYROPHOSPHATE
L6             3 S L4 AND HYDROLY? (4A) PYROPHOSPHATE

=> s l1 and destroy? (5a) fluorescen? (6a) remov?
L7             0 L1 AND DESTROY? (5A) FLUORESCEN? (6A) REMOV?

=> s l1 and destroy? (6a) fluoresce?
L8             1 L1 AND DESTROY? (6A) FLUORESCE?

=> d l8 bib abs

L8   ANSWER 1 OF 1  USPATFULL
AN     94:100500  USPATFULL
TI     Method and apparatus for automatic nucleic acid sequence determination
IN     Tibbetts, Clark, Nashville, TN, United States
       Bowling, John M., Murfreesboro, TN, United States
PA     Vanderbilt University, Nashville, TN, United States (U.S. corporation)
PI     US 5365455              19941115
AI     US 1991-763457          19910920 (7)
DT     Utility
FS     Granted
EXNAM  Primary Examiner: Harvey, Jack B.; Assistant Examiner: Choi, Jae H.
LREP   Needle & Rosenberg
CLMN   Number of Claims: 38
ECL    Exemplary Claim: 1
DRWN   16 Drawing Figure(s); 16 Drawing Page(s)
LN.CNT 1440
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
```

AB A method and system for automated nucleic acid sequence determination of a polynucleotide, wherein a **nucleic acid sequencing** ladder comprises signals corresponding to oligonucleotides formed from the polynucleotide, comprising the step of correlating, particularly in a trained neural network or a scatter plot, an intensity variable for each signal in the **nucleic acid sequencing** ladder with an informative variable for that signal, wherein the informative variable comprises information from at least two adjacent signals in the **nucleic acid sequencing** ladder, such that each signal in the **nucleic acid sequencing** ladder identified so as to determine the nucleic acid sequence corresponding to the polynucleotide. In particular, the relative separation between consecutive signals, the relative intensities between consecutive signals, and a pattern recognition factor, which incorporates a comparison of relative separations and intensities of at least two adjacent signals with pattern recognition templates, can be used as informative variables. Furthermore, this invention relates to a method and system for the on-the-fly resolution and extraction of information of signals contained in a digitized data stream involving calculation of the smoothed second derivative of a data point from the smoothed first derivative of the data point.

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d l8 kwic

L8 ANSWER 1 OF 1 USPATFULL

AB A method and system for automated nucleic acid sequence determination of a polynucleotide, wherein a **nucleic acid sequencing** ladder comprises signals corresponding to oligonucleotides formed from the polynucleotide, comprising the step of correlating, particularly in a trained neural network or a scatter plot, an intensity variable for each signal in the **nucleic acid sequencing** ladder with an informative variable for that signal, wherein the informative variable comprises information from at least two adjacent signals in the **nucleic acid sequencing** ladder, such that each signal in the **nucleic acid sequencing** ladder identified so as to determine the nucleic acid sequence corresponding to the polynucleotide. In particular, the relative separation between. . .

SUMM . . . the nucleic acid sequence and a process for extracting information on-the-fly from a digitized data stream that corresponds to the **nucleic acid sequencing** ladder.
Because the novel informative variables contain information concerning the identity of neighboring nucleotides in a polynucleotide, these variables can. . . process for resolving signals provided by this invention allows for more accurate detection of the characteristics of signals in a **nucleic acid sequencing** ladder, thus providing a method and system for accurately measuring these novel informative variables. Because the measurement and correlation of. . .

SUMM . . . a method and system for automated nucleic acid sequence determination in which an intensity variable for each signal in the **nucleic acid sequencing** ladder is correlated with an informative variable for that signal such that each signal in the **nucleic acid sequencing** ladder is identified to determine the nucleic acid sequence corresponding to the polynucleotide. The informative variable is a variable that comprises information from at least two adjacent signals in the **nucleic acid sequencing** ladder, such as the relative separation between two consecutive signals, the relative intensity between two consecutive signals, or a combination. . .

SUMM The electrophoretic separation of oligonucleotides in **nucleic acid sequencing** gels is primarily a function of length. However, as disclosed by this invention, the terminal nucleotides of an oligomer affect. . . mobility in a determinable fashion. Thus, the relative separation between adjacent signals, as determined for a particular signal in a **nucleic acid sequencing** ladder, contains information regarding the identity of terminal nucleotides, particularly the last 2-3 nucleotides, of the oligomer that corresponds to. . .

SUMM . . . system for enhanced resolution of signals contained in a digitized data stream comprising successive signals corresponding to oligonucleotides in a **nucleic acid sequencing** ladder formed from a nucleotide. According to this method, the second derivative smoothed over m data points of the first. . . stream. Because this time-linear process provides for rapid data processing, this method is also ideally suited in contexts other than **nucleic acid sequencing**, such as time-of-flight mass spectrometry.

SUMM . . . for nucleic acid, particularly DNA, sequence determination of a nucleotide by correlating an intensity variable for each signal in a

nucleic acid sequencing ladder with an
informative variable for that signal, wherein the informative variable comprises information from at least two adjacent signals in the **nucleic acid sequencing** ladder. The use of relative separation, relative intensity and a pattern recognition factor as informative variables in this method, either. . .

SUMM . . . a polynucleotide from a digitized data stream in which the data stream comprises successive signals corresponding to oligonucleotides in a **nucleic acid sequencing** ladder formed from a polynucleotide. Thus, it is an object of this invention to provide a system including means for. . .

DETD . . . both streams divided by the sum of the intensities in both streams, can be obtained easily. For instance, in the **nucleic acid sequencing** context, the intensity of a signal from one data channel corresponds to the yield of a particular oligomer and the. . .

DETD Thus, the on-the-fly second derivative procedure does not **destroy** the **fluorescence** spectrochemical integrity that allows primary identification of the various bases. However, in addition to treating the fluorescence labeling of signals. . .

DETD . . . of the primary data streams provides partially deconvolved arrays of fluorescence and mobility data for sequences of oligomers in the **nucleic acid sequencing** context.
Furthermore, this method is also very effective in a wide variety of applications beyond DNA sequencing analysis, particularly in. . .

DETD Use of Electrophoretic Separations Between Successive Oligomers as an Informative Variable in **Nucleic Acid Sequencing**

DETD The instant invention provides for an improved method and apparatus for **nucleic acid sequencing** by identifying and implementing new informative components of **nucleic acid sequencing** ladders in addition to the primary determinative variables such as lane position or fluorescence ratios. One such informative variable is the relative separations of successive oligomers in the **nucleic acid sequencing** ladders. As used herein, the term "relative separation(s)" for an adjacent pair of oligomers refers to either the spatial distance. . .

DETD Electrophoretic separation of oligonucleotides in **nucleic acid sequencing** gels, such as denaturing polyacrylamide gels, is primarily a function of length-dependent mobility. However, as is described in our paper,. . .

DETD Use of Relative Oligomer Yields as an Informative Variable in **Nucleic Acid Sequencing**

DETD . . . in FIG. 5, not only does the local nucleic acid sequence affect the relative separations of successive oligomers in the **nucleic acid sequencing** ladders, a particular nucleotide also affects the yields of oligomers at neighboring positions. FIG. 5 overlays the signal profiles from. . .

CLM What is claimed is:
1. A method for the nucleic acid sequence determination of a polynucleotide, wherein a **nucleic acid sequencing** ladder comprises signals corresponding to oligonucleotides formed from the polynucleotide, comprising the step of correlating an intensity variable for each signal in the **nucleic acid sequencing** ladder with an informative variable for that signal, wherein the informative variable comprises information from at least two adjacent signals from other than a tri-nucleotide palindrome in the **nucleic acid sequencing** ladder, such that each signal in the **nucleic acid sequencing** ladder is identified so as to determine the nucleic acid sequence corresponding to the polynucleotide.

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. . . acid sequencer, wherein the data stream comprises successive signals corresponding to oligonucleotides from other than a tri-nucleotide palindrome in a **nucleic acid sequencing** ladder formed from the polynucleotide; b) locating the position of the maximum for each signal in the data stream; c). . . data stream, wherein the informative variable comprises position of maxima or intensities for at least two adjacent signals in the **nucleic acid sequencing** ladder; and c) correlating the informative variable for each signal with the intensity variable for each signal to determine the. . .

. . . comprising the steps of acquiring an intensity variable and at least one informative variable for each signal contained in a **nucleic acid sequencing** ladder corresponding to the polynucleotide and correlating in a trained neural network the intensity variable and the at least one. . .

. . . comprising the steps of acquiring an intensity variable and at least one informative variable for each signal contained in a **nucleic acid sequencing** ladder corresponding to the polynucleotide and correlating in a trained neural network the intensity variable and the at least one. . .

. . . stream, wherein the digitized data stream comprises successive signals corresponding to oligonucleotides from other than a tri-nucleotide palindrome in a **nucleic acid sequencing** ladder formed from the polynucleotide, comprising: a) means for calculating an intensity variable for each signal in the digitized data. . . signal in the digitized data stream, wherein the informative variable comprises information from at least two adjacent signals in the **nucleic acid sequencing** ladder; and c) means for correlating the intensity for each signal with the informative variable for each signal to identify each signal in the **nucleic acid sequencing** ladder so as to determine the nucleic acid sequence corresponding to the polynucleotide.

. . . acid sequencer, wherein the data stream comprises successive signals corresponding to oligonucleotides from other than a tri-nucleotide palindrome in a **nucleic acid sequencing** ladder formed from the polynucleotide; b) means for calculating the position of the maximum for each signal; c) a memory. . . signal in the digitized data stream, wherein the informative variable comprises information from at least two adjacent signals in the **nucleic acid sequencing** ladder; g) means for storing in the memory the informative variable for each signal; h) means for retrieving the intensity. . . correlate the intensity variable for each signal and the informative variable for each signal to identify each signal in the **nucleic acid sequencing** ladder so as to determine the nucleic acid sequence corresponding to the polynucleotide.

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